REMARKS

Claims 1-22 are pending in the application. Claims 4-8, 21, and 22 have been withdrawn from consideration. Claims 1, 14, 17, and 20 have been amended, claim 16 has been cancelled, and claims 23-27 have been added. Accordingly, Claims 1-3, 9-15, 17-20, and 23-27 are currently under consideration.

Support for amendment of claim 1 can be found, for example, in the original claims and paragraphs [0027], [0061], [0066], and [0067] of the Specification. Claim 14 is amended to substitute "said patient" for "a patient." Support for amendment of claim 17 can be found, for example, in the original claims and paragraphs [0015], [0027], [0066], and [0067] of the Specification. Support for amendment of claim 20 can be found, for example, in the original claims and paragraphs [0027], [0066], and [0067] of the Specification. Support for new claims 23-27 can be found, for example, in paragraphs [0066] and [0067] of the Specification. No new matter is added.

With respect to the cancellation and amendment of claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

35 USC § 112

35 USC § 112, first paragraph

Claims 1-3 and 9-20 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for a method of prevention. Applicants respectfully traverse this rejection.

Without acquiescing to the Examiner's statement and solely to expedite prosecution, Applicants have amended independent claims 1, 17, and 20 to substitute "attenuate symptoms, and/or delay progression of the disease state of heart failure" for "prevent exacerbation of

symptoms, and/or prevent and/or delay progression of the disease state of heart failure," thus obviating the rejection.

In view of the foregoing, Applicants respectfully request that the rejection under 35 USC § 112, first paragraph, be withdrawn.

35 USC § 112, second paragraph

Claims 17-19 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite regarding the terms "several" in claim 17 and "improves the quality of life" in claim 19. Applicants respectfully traverse this rejection.

Solely to expedite prosecution, Applicants have amended claim 17 to delete "several times," thus obviating the rejection of claims 17 and 18.

With respect to the phrase "improves the quality of life" in claim 19, Applicants wish to direct the Examiner's attention to paragraph [0028] of the Specification, where it states:

> This invention also provides a method of improving the quality of life in a patient with HF. "Quality of life" refers to one or more of a person's ability to walk, climb stairs, do errands, work around the house, participate in recreational activities, and/or not requiring frequent rest intermittently during activities, and/or the absence of sleeping problems or shortness of breath.

Thus, the term "quality of life" is clearly defined in the Specification. One of ordinary skill in the art would readily understand what the term "improves the quality of life" means, and ascertain and confirm that quality of life has been improved.

In view of the foregoing, Applicants respectfully request that the rejection under 35 USC § 112, second paragraph, be withdrawn.

Claim Rejections – 35 USC § 103

Rejection under 35 USC § 103(a) of claims 1, 2 and 10-20 over Stevenson, Anand, Shekhar and Gennari

Claims 1, 2 and 10-20 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stevenson (Int J Cardiol. 1992, 37(3):407-14), Anand (J Am Coll Cardiol. 1991, 17(1):208-17), Shekhar (J Cardiol. 1991, 67(8):732-6) and Gennari (Cardiovasc Res. 1990, 24(3):239-41). Applicants respectfully traverse this rejection.

Without acquiescing to the Examiner's statement and solely to expedite prosecution, Applicants have amended independent claims 1 and 20 to recite "said treatment is followed by a maintenance therapy comprising administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure."

The Examiner acknowledges that Stevenson, Anand, Shekhar, and Gennari do not teach the specific dosages for the specific times recited in claims 1, 16, 17, and 20. Office Action at page 6. Moreover, claims 1 and 20 as amended require the use of a maintenance therapy. None of the cited references, namely, Stevenson, Anand, Shekhar, and Gennari, teach or suggest a maintenance therapy, much less a maintenance therapy comprising administration of CGRP at a low dose, e.g., at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure, as required by amended claims 1 and 20.

Specifically, Stevenson discloses the administration of CGRP at 600 ng/min by a continuous 48-hour infusion or 8-hour infusion at the start of the 2 study days. See Stevenson, page 408, right column, the first full paragraph to the third full paragraph.

Anand discloses the infusion of human α-CGRP at 0.8, 3.2, and 16 ng/kg/min for 10 minutes for the first two doses and 20 minutes for the third dose to patients with age of 17 to 50 years. See Anand, the paragraph bridging page 208 to page 209; page 209, the paragraph bridging the left column and the right column.

Shekhar discloses the intravenous infusion of CGRP at 8.0 ng/kg/min for 8 hours to patients with age of 52±3 years. See Shekhar, page 733, left column, the first paragraph.

Gennari discloses the intravenous infusion of human CGRP II (or β) at 12.5 ug/h, i.e., 208.3 ng/min, for 24 hours to patients with body weight of 44-66 kg. See Gennari, page 239, right column, the first full paragraph to the second full paragraph.

None of the references teach or suggest administering CGRP "at a rate between about 50 and 500 ng/min for a time between 30 minutes and 8 hours per day as needed to provide symptomatic relief, attenuate symptoms, and/or delay progression of the disease state of heart failure" or "a maintenance therapy comprising administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure," as recited in amended claim 1.

With respect to independent claim 17, Applicants have amended claim 17 to recite "said treatment is optionally followed by a maintenance therapy comprising administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure." The cited references are discussed above. None of the cited references, namely, Stevenson, Anand, Shekhar, and Gennari, alone or in combination, teach or suggest administering CGRP "at a rate between about 500 and 600 ng/min for up to 8 hours per day for at least three consecutive days per week as needed to provide symptomatic relief, attenuate symptoms, and/or delay progression of the disease state of heart failure" or an optional maintenance therapy comprising "administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure," as recited in amended claim 17.

Therefore, independent claims 1, 17, and 20 as amended are not obvious over the cited references. Claims 2 and 10-15 and claims 18-19 depend from claims 1 and 17, respectively, and are not obvious at least for the reasons that independent claims 1 and 17 as amended are not obvious over the cited references.

In addition, as discussed above, none of the cited references, Stevenson, Anand, Shekhar, and Gennari, alone or in combination, teach or suggest administering CGRP "at a rate between about 0.8 to 10 ng/min," as recited in newly added claim 26. Moreover, none of the cited references, Stevenson, Anand, Shekhar, and Gennari, alone or in combination, teach or suggest a long term maintenance therapy, e.g., administering maintenance therapy "over a period of 3, 6, or 9 months" as recited in newly added claims 23-25 and 27.

In view of the foregoing, Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 USC § 103(a) of claims 1 and 3 over Stevenson, Anand, Shekhar and Gennari and further in view of Heim, Young, Strom, and Torgerson

Claims 1 and 3 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stevenson, Anand, Shekhar and Gennari as applied to claim 1, and further in view of Heim (U.S. Patent No. 5,126,134), Young (U.S. Patent No. 4,627,839), Strom (U.S. Patent No. 5,336,489) and Torgerson (U.S. Patent No. 5,820,589). Applicants respectfully traverse this rejection.

As discussed above, none of the primary references, namely, Stevenson, Anand, Shekhar, and Gennari, alone or in combination, teach or suggest a maintenance therapy, much less a maintenance therapy comprising administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure, as required by amended claim 1. Even in view of the secondary references, namely, Heim, Young, Strom and Torgerson, there is no teaching or suggestion of the use of a maintenance therapy comprising administration of CGRP at a low dose, e.g., at a rate between about 0.8 to 10 ng/min.

The Examiner acknowledges that Heim, Young, Strom and Torgerson do not teach the infusion of CGRP to heart failure patients. See Office Action at page 8. The secondary references are cited as allegedly disclosing "a constant rate infusion pump" (Heim, column 14, lines 4-5), "programmable infusion pumps" (Young, column 1, lines 10-15), "Alzet osmotic pumps" (Strom, column 6, lines 41-45), and "fixed- or variable- rate pumps" (Torgerson, column 1, lines 15-20).

None of the secondary references provide the suggestion of a low dose administration of CGRP at a rate between about 0.8 to 10 ng/min. Specifically, Heim discloses a pharmaceutical composition comprising a plasminogen activator and hirudin together with a pharmaceutically acceptable carrier. See Abstract. Young discloses a removable cover for converting a programmable infusion pump into a patient-controlled analgesia device. See Abstract. Strom is related to a method of lysing unwanted, non-malignant cells in a mammal. See Abstract. Torgerson is related to an implantable pump. See Abstract. None of Heim, Young, Strom and Torgerson teach or suggest administration of CGRP at a rate between about 0.8 to 10 ng/min, thus they do not cure the deficiencies of the primary references, Stevenson, Anand, Shekhar, and Gennari.

Therefore, claim 1 as amended is not obvious over Stevenson, Anand, Shekhar, and Gennari in view of Heim, Young, Strom and Torgerson.

Claim 3 depends from claim 1 and recites the administration of CGRP via a constant rate pump, a variable rate pump, a programmable pump, or an osmotic pump. As discussed above, claim 1 is not obvious over the cited references. For the same reasons, claim 3 that depends from claim 1 is not obvious over the cited references.

In view of the foregoing, Applicants respectfully request that this rejection be withdrawn.

Rejection under 35 USC § 103(a) of claims 1 and 9 over Stevenson, Anand, Shekhar and Gennari and further in view of Chen

Claims 1 and 9 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stevenson, Anand, Shekhar and Gennari as applied to claim 1 above, and further in view of Chen (U.S. Patent No. 6,525,102). Applicants respectfully traverse this rejection.

As discussed above, none of the primary references, namely, Stevenson, Anand, Shekhar, and Gennari, alone or in combination, teach or suggest a maintenance therapy, much less a maintenance therapy comprising administration of CGRP at a rate between about 0.8 to 10 ng/min to relieve or attenuate symptoms or delay progression of said heart failure, as required by amended

claim 1. Even in view of the secondary reference, Chen, there is no teaching or suggestion of the use of a maintenance therapy comprising administration of CGRP at a low dose, e.g., at a rate between about 0.8 to 10 ng/min.

The Examiner acknowledges that Chen does not teach the infusion of CGRP to heart failure patients. See Office Action at page 9. Chen is cited as allegedly disclosing the use of surfactant for stabilizing and/or protecting the polypeptide.

Chen does not provide the suggestion of a low dose administration of CGRP at a rate between about 0.8 to 10 ng/min. Specifically, Chen is related to a pharmaceutical composition comprising an amino acid base, which serves as the primary stabilizing agent of the polypeptide, and an acid and/or its salt form to buffer the solution within an acceptable pH range for stability of the polypeptide. See Abstract. Chen does not teach or suggest administration of CGRP at a rate between about 0.8 to 10 ng/min, thus it does not cure the deficiencies of the primary references, Stevenson, Anand, Shekhar, and Gennari.

Therefore, claim 1 as amended is not obvious over Stevenson, Anand, Shekhar, and Gennari in view of Chen.

Claim 9 depends from claim 1 and recites the combination of CGRP with one or more agents selected from the group consisting of alcohols, moisturizers, humectants, oils, emulsifiers, thickeners, thinners, surface active agents, fragrances, preservatives, antioxidants, vitamins, and minerals. As discussed above, claim 1 is not obvious over the cited references. For the same reasons, claim 9 that depends from claim 1 is not obvious over the cited references.

In view of the foregoing, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 560252000800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: May 21, 2010

Respectfully submitted,

Electronic Signature: /Lina Zhang/
Lina Zhang
Registration No.: 58956
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304-1018
(650) 813-5840